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Substitute for form 1449/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use as many sheets as necessary)				Application Number	09/506,079
				Filing Date	February 16, 2000
				First Named Inventor	Gail M. Clinton
				Art Unit	1643
				Examiner Name	Anne L. Holleran
Sheet	1	of	17	Attorney Docket Number	49321-16

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>1</sup> (if known)			
		US-4,376,110	03-08-1983	David et al.	
		US-4,777,127	10-11-1988	Suni et al.	
		US-4,946,778	08-07-1990	Ladner et al.	
		US-4,959,314	09-25-1990	Mark et al.	
		US-5,149,655	09-22-1992	McCabe et al.	
		US-5,206,152	04-27-1993	Sukhatme	
		US-5,219,740	06-15-1993	Miller et al.	
		US-5,422,120	06-06-1995	Kim	
		US-5,580,859	12-03-1996	Felgner et al.	
		US-5,705,157	01-06-1998	Greene et al.	
		US-5,720,954	02-24-1998	Hudziak et al.	
		US-5,772,997	06-30-1998	Hudziak et al.	
		US-5,811,098	09-22-1998	Plowman et al.	
		US-5,814,482	09-29-1998	Dubensky, Jr. et al.	
		US-5,876,712	03-02-1999	Cheever et al.	
		US-6,331,526	12-18-2001	Baserga et al.	
		US-6,337,338	01-08-2002	Kozlowski et al.	
		US-6,340,674	01-22-2002	Baserga et al.	
		US-6,541,214	04-01-2003	Clinton	
		US-6,673,343	01-06-2004	Bennett et al.	
		US-6,841,367	01-11-2005	Kendall et al.	
		US-7,125,680	10-24-2006	Singer et al.	
		US-2002/0064785	05-30-2002	Mass	
		US-2002/0173458	11-21-2002	Ruben et al.	
		US-2003/0059863	03-27-2003	Clinton	
		US-2003/0105051	06-05-2003	McSwiggen	
		US-2003/0157097	08-21-2003	Noguchi et al.	
		US-2003/0171278	09-11-2003	Dennis	

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				Examiner Name	Anne L. Holleran
				Attorney Docket Number	49321-16
Sheet	2	of	17		

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		US-2003/0228663	12-11-2003	Lowman et al.		
		US-2003/0235556	12-25-2003	Wolin et al.		
		US-2004/0022785	02-05-2004	Clinton et al.		
		US-2004/0023887	02-05-2004	Pillutla et al.		
		US-2004/0052796	03-18-2004	Clinton		
		US-2004/0082510	04-29-2004	Ullrich et al.		
		US-2004/0106161	06-03-2004	Bossenmaier et al.		
		US-2004/0142931	07-22-2004	Vite et al.		
		US-2004/0242684	12-02-2004	Chen et al.		
		US-2005/0239088	10-27-2005	Shepard et al.		

  

FOREIGN PATENT DOCUMENTS						
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		AU 777422	10-14-2004	Oregon Health Sciences University		
		AU 777803	10-28-2004	Oregon Health Sciences University		
		CA 2,418,083	02-14-2002	Imclone Systems, Inc.		
		CN 1607247	04-20-2005	Shanghai Haixin Bio Tech Co Lt (CN)		
		EP 0345242	12-06-1989	SmithKline Biolog (BE)		
		EP 0524968	02-03-1993	Research Development Foundation		
		GB 2200651	08-10-1988	Al Sumidaie Ayad Mohamed Khala		
		WO 90/07936	07-26-1990	Chiron Corporation		
		WO 90/11092	10-04-1990	Vical, Inc.		
		WO 91/02805	03-07-1991	Viagene, Inc.		
		WO 91/11715	08-08-1991	State of Oregon		

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		WO 91/14445	10-03-1991	Research Development Foundation		
		WO 92/11033	07-09-1992	Arch Development Corporation		
		WO 93/03769	03-04-1993	The United States of America		
		WO 93/10218	05-27-1993	The United States Government		
		WO 93/11230	06-10-1993	Dynal AS		
		WO 93/14778	08-05-1993	Vical, Inc.		
		WO 93/19191	09-30-1993	Centre National de la Recherche Scientifique		
		WO 93/25234	12-23-1993	The Regents of the University of California		
		WO 93/25698	12-23-1993	The United States Government		
		WO 94/03622	02-17-1994	Imperial College of Science		
		WO 94/12649	06-09-1994	Genzyme Corporation		
		WO 94/23697	10-27-1994	Depotech Corporation		
		WO 94/28938	12-22-1994	The Regents of the University of Michigan		
		WO 95/00655	01-05-1995	Mc Master University		
		WO 95/07994	03-23-1995	Viagene, Inc.		
		WO 95/11984	05-04-1995	Canji, Inc.		
		WO 95/13796	05-26-1995	Depotech Corporation		
		WO 95/30763	11-16-1995	Viagene, Inc.		
		WO 96/17072	06-06-1996	Chiron Viagene, Inc.		
		WO 97/18241	05-22-1997	Thomas Jefferson University		
		WO 97/42338	11-13-1997	Chiron Corporation		
		WO 00/29609	05-25-2000	Oregon Health Sciences University		

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		WO 00/35455	06-22-2000	Telik, Inc.		
		WO 00/44403	08-03-2000	Oregon Health Sciences University		
		WO 01/61356	08-23-2001	Oregon Health Sciences University		
		WO 02/12335	02-14-2002	Pharmacia Corporation		
		WO 02/14470	02-21-2002	Oregon Health and Science University		
		WO 03/061571	07-31-2003	Chiron Corporation		
		WO 03/070747	08-28-2003	Novo Nordisk		
		WO 2004/041065	05-21-2004	The United States of America		
		WO 2004/054996	07-01-2004	Axelar AB		
		WO 2004/055022	07-01-2004	Axelar AB		
		WO 2005/016966	02-24-2005	Receptor BioLogix, Inc.		
		WO 2005/112969	12-01-2005	Oregon Health and Science University		
		WO 2006/042002	04-20-2006	Oregon Health and Science University		

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		ADACHI et al., "Effects of Genetic Blockage of the Insulin-like Growth Factor Receptor in Human Colon Cancer Cell Lines," Gastroenterology 123(4):1191-1204, October 2002	
		AHMAD, et al., "The Mitogenic Action of Insulin-like Growth Factor I in Normal Human Mammary Epithelial Cells Requires the Epidermal Growth Factor Receptor Tyrosine Kinase," Journal of Biological Chemistry 279(3):1713-1719, January 16, 2004	
		ALBANELL et al., "Mechanism of Action of Anti-HER2 Monoclonal Antibodies: Scientific Update on Trastuzumab and 2C4," New Trends in Cancer for the 21 <sup>st</sup> Century, Kluwer Academic/Plenum Publishers, New York, pp. 253-268, 2003	
		ANDREWS et al., "Results of a Pilot Study Involving the Use of an Antisense Oligodeoxynucleotide Directed Against the Insulin-Like Growth Factor Type I Receptor in Malignant Astrocytomas," Journal of Clinical Oncology 19(8):2189-2200, April 15, 2001	

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		ARIHIRO et al., "Expression of CD31, Met/hepatocyte growth factor receptor and bone morphogenetic protein in bone metastasis of osteosarcoma," Pathology International 51:100-106, 2001	
		AZUMA et al., "Identification of HER2/neu-derived peptides capable of inducing both cellular and humoral immune responses in HLA-A24 positive breast cancer patients," Breast Cancer Reserch and Treatment 86(1):19-29, July 2004	
		BAASNER et al., "Reversible tumorigenesis in mice by conditional expression of the HER2c-erbB2 receptor tyrosine kinase," Oncogene 13(5):901-11, 1996	
		BARGMAN et al., "Oncogenic activation of the neu-encoded receptor protein by point mutation and deletion," EMBO Journal 7(7):2043-2052, 1988	
		BASELGA et al., "Phase II Study of Weekly Intravenous Recombinant Humanized Anti-p185(HER2) Monoclonal Antibody in Patients With HER2/neu-Overexpressing Metastatic Breast Cancer," Journal of Clinical Oncology 14(3):737-744, 1996	
		BASERGA, "Haystacks and Needles," Human Pathology 31(3):275-276, March 2000	
		BASU et al., "Inhibition of tyrosine kinase activity of the epidermal growth factor (EGF) receptor by a truncated receptor form that binds to EGF: role for interreceptor interaction in kinase regulation," Mol. Cell. Biol. 9:671-677, 1989	
		BAZLEY et al., "The epidermal growth factor receptor family," Endocrine-Related Cancer 12:S17-S27, 2005	
		BEECH et al., "Insulin-like growth factor-I receptor antagonism results in increased cytotoxicity of breast cancer cells to doxorubicin and taxol," Oncology Reports 8(2):325-329, March-April 2001	
		BENINI et al., "Inhibition of Insulin-like Growth Factor I Receptor Increases the Antitumor Activity of Doxorubicin and Vincristine against Ewing's Sarcoma Cells," Clinical Cancer Research 7(6):1790-1797, June 2001	
		BIRD, "Single-Chain Antigen-Binding Proteins," Science 242:423-426, 1988	
		BLUME-JENSEN et al., "Oncogenic kinase signalling," Nature 411(6835):355-365, May 17, 2001	
		BOHULA et al., "Targeting the type 1 insulin-like growth factor receptor as anti-cancer treatment," Anticancer Drugs 14(9):669-682, October 2003	
		BOND et al., "Cloning and functional expression of the cDNA encoding an inwardly-rectifying potassium channel expressed in pancreatic beta-cells and in the brain," FEBS Letters 367:61-66, 1995	
		BORK, "Powers and pitfalls in sequence analysis: the 70% hurdle," Genome Research 10:398-400, 2000	
		BRANDON et al., "Estrogen Receptor Gene Expression in Human Uterine Leiomyomata," J. Clin. Endocrinol. Metab. 80(6):1876-1881, 1995	
		BRANDON et al., "Progesterone receptor messenger ribonucleic acid and protein are overexpressed in human uterine leiomyomas," American Journal of Obstetrics and Gynecology 169(1):78-85, 1993	
		BRODOWICZ et al., "Soluble HER-2/neu Neutralizes Biologic Effects of Anti-HER-2/neu Antibody on Breast Cancer Cells in Vitro," Int. J. Cancer 73:875-879, 1997	
		BROWN et al., "Antibodies against Highly Conserved Sites in the Epidermal Growth Factor Receptor Tyrosine Kinase Domain as Probes for Structure and Function," Biochemistry 32:4659-4664, 1993	
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		BURTRUM et al., "A Fully Human Monoclonal Antibody to the Insulin-Like Growth Factor I Receptor Blocks Ligand-Dependent Signaling and Inhibits Human Tumor Growth in Vivo," Cancer Research 63(24):8912-8921, December 15, 2003	
		BYRON et al., "Potential Therapeutic Strategies to Interrupt Insulin-Like Growth Factor Signaling in Breast Cancer," Seminars in Oncology 30(5 Suppl 16):125-132, October 2003	
		CAMIRAND et al., "Co-targeting HER2/ErbB2 and insulin-like growth factor-1 receptors causes synergistic inhibition of growth in HER2-overexpressing breast cancer cells," Med Sci Monit 8(12):BR521-526, December 2002	
		CAMIRAND et al., "Co-targeting IGF-IR and c-kit: synergistic inhibition of proliferation and induction of apoptosis in H 209 small cell lung cancer cells," British Journal of Cancer 90(9):1825-1829, May 4, 2004	
		CAMP et al., "Molecular Mechanisms of Resistance to Therapies Targeting the Epidermal Growth Factor Receptor," Clinical Cancer Research 11(1):397-405, January 1, 2005	
		CAMPIGLIO et al., "Inhibition of Proliferation and Induction of Apoptosis in Breast Cancer Cells by the Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitor ZD1839 (Iressa) Is Independent of EGFR Expression Level," Journal of Cellular Physiology 198(2):259-268, February 2004	
		CARRAWAY et al., "A Neu Acquaintance for ErbB3 and ErbB4: A Role for Receptor Heterodimerization in Growth Signaling," Cell 78(5-8), 1994	
		CARTER et al., "Tissue-Specific Transformation by Oncogenic Mutants of Epidermal Growth Factor Receptor," Critical Review in Oncogenesis 5(4):389-428, 1994	
		CHAKRAVARTI et al., "Insulin-like Growth Factor Receptor I Mediates Resistance to Anti-Epidermal Growth Factor Receptor Therapy in Primary Human Glioblastoma Cells through Continued Activation of Phosphoinositide 3-Kinase Signaling," Cancer Research 62(1):200-207, January 1, 2002	
		CHANG, "Enhanced Efficacy of DNA Vaccination Against Her-2/neu Tumor Antigen by Genetic Adjuvants," International Journal of Cancer 111(1):86-95, August 10, 2004	
		CHIU et al., "Tumor-targeted gene delivery via anti-HER2 antibody (trastuzumab, Herceptin®) conjugated polyethylenimine," Journal of Controlled Release 97(2):357-369, June 18, 2004	
		CHRISTIANSEN et al., "Biological impediments to monoclonal antibody-based cancer immunotherapy," Molecular Cancer Therapeutics 3(11):1493-1501, November 2004	
		CLELAND et al., "The Development of Stable Protein Formulations: A Close Look at Protein Aggregation, Deamidation, and Oxidation," Critical Reviews in Therapeutic Drug Carrier Systems 10(4):307-377, 1993	
		CLINTON et al., "Estrogen action in human ovarian cancer," Crit. Rev. Oncol/Hematol. 25:1-9, 1997	
		CLINTON et al., "Estrogens increase the expression of fibulin-1, an extracellular matrix protein secreted by human ovarian cancer cells," Proc. Natl. Acad. Sci. 93:316-320, 1996	
		CLINTON et al., "Generation and Use of Anti-peptide Antibodies Directed against Catalytic Domain of Protein Kinases," Methods in Enzymology 200:463-474, 1991	

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		Art Unit	1643
		Examiner Name	Anne L. Holleran
		Attorney Docket Number	49321-16
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		CODONY-SERVAT et al., "Cleavage of the HER2 ectodomain is a pervanadate-activable process that is inhibited by the tissue inhibitor of metalloproteases-1 in breast cancer cells," Cancer Res. 59(6):1196-1201, 1999	
		COLE et al., "The EBV-Hybridoma Technique and Its Application to Human Lung Cancer," Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc., pp. 77-96, 1985	
		CONNELLY et al., "In Vivo Gene Delivery and Expression of Physiological Levels of Functional Human Factor VIII in Mice," Human Gene Therapy 6(2):185-193, February 1995	
		COTE et al., "Generation of human monoclonal antibodies reactive with cellular antigens," Proc. Natl. Acad. Sci. 80:2026-2030, 1983	
		CUNNINGHAM et al., "High-Resolution Epitope Mapping of hGH-Receptor Interactions by Alanine-Scanning Mutagenesis," Science 244(4908):1081-1085, June 2, 1989	
		CURIEL et al., "High-Efficiency Gene Transfer Mediated by Adenovirus Coupled to DNA-Polylysine Complexes," Human Gene Therapy 3(2):147-154, April 1992	
		CURTI, "Physical barriers to drug delivery in tumors," Critical Reviews in Oncology/Hematology 14:29-39, 1993	
		DATABASE, Database accession No. P04626, ERB2_HUMAN, "Receptor tyrosine-protein kinase erbB-2 precursor," created 8/13/87, <a href="http://www.ebi.uniprot.org/uniprot-srv/uniProtView.do?proteinID=ERB2_HUMAN&amp;pager.offset=null">www.ebi.uniprot.org/uniprot-srv/uniProtView.do?proteinID=ERB2_HUMAN&amp;pager.offset=null</a>	
		DATTA et al., "Cellular survival: a play in three Acts," Genes & Development 13:2905-2927, November 1999	
		DE GIOVANNI et al., "Immunoprevention of HER-2/neu Transgenic Mammary Carcinoma through an Interleukin 12-Engineered Allogeneic Cell Vaccine," Cancer Research 64(11):4001-4009, June 1, 2004	
		DEGRENDELE et al., "The Anti-HER2 Monoclonal Antibody Pertuzumab May Be Effective in Androgen-Independent Prostate Cancer," Clinical Prostate Cancer 2(3):143-145, December 2003	
		DENNY, "Prodrug strategies in cancer therapy," Eur. J. Med. Chem. 36(7-8):577-595, July-August 2001	
		DERMER, "Another Anniversary for the War on Cancer," Bio/Technology 12:320, 1994	
		DE VOS, "Human Growth Hormone and Extracellular Domain of Its Receptor: Crystal Structure of the Complex," Science 255(5042):306-312, January 17, 1992	
		DI FIORE et al., "erbB-2 Is a Potent Oncogene When Overexpressed in NIH/3T3 Cells," Science 237:178-182, 1987	
		DILLMAN, "Antibodies as Cytotoxic Therapy," J. Clin. Oncol. 12(7):1497-1515, 1994	
		DOHERTY et al., "An Alternative HER-2/neu Transcript of 8 kb Has an Extended 3'UTR and Displays Increased Stability in SKOV-3 Ovarian Carcinoma Cells," Gynecologic Oncology 74(3):408-415, 1999	
		DOUGALL et al., "The neu-oncogene: signal transduction pathways, transformation mechanisms and evolving therapies," Oncogene 9:2109-2123, 1994	
		EARP et al., "Heterodimerization and functional interaction between EGF receptor family members: A new signaling paradigm with implications for breast cancer research," Breast Cancer Research and Treatment 35:115-132, 1995	

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		EKSTRAND et al., "Amplified and rearranged epidermal growth factor receptor genes in human glioblastomas reveal deletions of sequences encoding portions of the N- and/or C-terminal tails," Proc. Natl. Acad. Sci. 89:4309-4313, May 1992	
		FILMUS et al., "Amplified, Overexpressed and Rearranged Epidermal Growth Factor Receptor Gene In A Human Astrocytoma Cell Line," Biochemical and Biophysical Research Communications 131(1):207-215, August 30, 1985	
		FILMUS et al., "MDA-468, A Human Breast Cancer Cell Line With A High Number Of Epidermal Growth Factor (EGF) Receptors, Has An Amplified EGF Receptor Gene And Is Growth Inhibited By EGF," Biochemical and Biophysical Research Communications 128(2):898-905, April 30, 1985	
		FINDEIS et al., "Targeted delivery of DNA for gene therapy via receptors," Trends Biotechnol. 11(5):202-205, May 1993	
		FITZPATRICK et al., "Formation of a high affinity heregulin binding site using the soluble extracellular domains of ErbB2 with ErbB3 or ErbB4," FEBS Letters 431:102-106, 1998	
		FLICKINGER et al., "An alternatively processed mRNA from the avian c-erbB gene encodes a soluble, truncated form of the receptor that can block ligand-dependent transformation," Mol. Cell. Biol. 12:883-893, 1992	
		GARRETT et al., "Crystal Structure of a Truncated Epidermal Growth Factor Receptor Extracellular Domain Bound to Transforming Growth Factor Alpha," Cell 110(6):763-773, September 20, 2002	
		GILBERT et al., "Targeted prodrug treatment of HER-2-positive breast tumor cells using trastuzumab and paclitaxel linked by A-Z-CINN™ Linker," Journal of Experimental Therapeutics and Oncology 3(1):27-35, January-February 2003	
		GILLOGLY et al., "li-Key/HER-2/neu MHC class-II antigenic epitope vaccine peptide for breast cancer," Cancer Immunol. Immunother. 53(6):490-496, June 2004	
		GIRNITA et al., "Cyclolignans as Inhibitors of the Insulin-Like Growth Factor-I Receptor and Malignant Cell Growth," Cancer Research 64(1):236-242, January 1, 2004	
		GRANERUS et al., "Effects of Insulin-Like Growth Factor-Binding Protein 2 And An IGF-Type I Receptor-Blocking Antibody On Apoptosis In Human Teratocarcinoma Cells In Vitro," Cell Biology International 25(8):825-828, 2001	
		GREENSPAN et al., "Defining epitopes: It's not as easy as it seems," Nature Biotechnol. 17:936-937, 1999	
		GREENSPAN et al., "Idiotypes: structure and immunogenicity," FASEB J. 75:437-444, 1993	
		GROENEN et al., "Structure-Function Relationships for the EGF/TGF-Alpha Family of Mitogens," Growth Factors 11:235-257, 1994	
		GRZMIL et al., "Blockade of the type I IGF receptor expression in human prostate cancer cells inhibits proliferation and invasion, up-regulates IGF binding protein-3, and suppresses MMP-2 expression," J. Pathol. 202(1):50-59, January 2004	
		GURA, "Systems for Identifying New Drugs Are Often Faulty," Science 278:1041-1042, 1997	
		HANSEN, "Re-examination and further development of a precise and rapid dye method for measuring cell growth/cell kill," Journal of Immunological Methods 119:203-210, 1989	
		HELDIN et al., "Ligand-induced Dimerization of Growth Factor Receptors: Variations on the Theme," Cytokine Growth Factor Reviews 7(1):3-10, 1996	

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		HELLAWELL et al., "Chemosensitization of human prostate cancer using antisense agents targeting the type 1 insulin-like growth factor receptor," BJU International 91(3):271-277, February 2003	
		HONGO et al., "Antitumor Effects of a Soluble Insulin-Like Growth Factor I Receptor in Human Ovarian Cancer Cells: Advantage of Recombinant Protein Administration in Vivo," Cancer Research 63(22):7834-7839, November 15, 2003	
		HU et al., "In Vivo Identification of the Interaction Site of ErbB2 Extracellular Domain With its Autoinhibitor," Journal of Cellular Physiology 205:335-343, 2005	
		HU et al., "Sequestering ErbB2 in endoplasmic reticulum by its autoinhibitor from translocation to cell surface: An autoinhibition mechanism of ErbB2 expression," Biochemical and Biophysical Research Communications 342(1):19-27, 2006	
		HUA et al., "SKOV3 Ovarian Carcinoma Cells Have Functional Estrogen Receptor but are Growth-resistant to Estrogen and Antiestrogens," J. Steroid Biochem. Molec. Biol. 55(3/4):279-289, 1995	
		HUDZIAK et al., "Increased expression of the putative growth factor receptor p185/HER2 causes transformation and tumorigenesis of NIH 3T3 cells," Proc. Natl. Acad. Sci. 84(20):7159-7163, 1987	
		HURWITZ et al., "Suppression and promotion of tumor growth by monoclonal antibodies to ErbB-2 differentially correlate with cellular uptake," Proc. Natl. Acad. Sci. 92(8):3353-3357, 1995	
		HUSE et al., "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," Science 246(4935):1275-1281, 1989	
		HUSTON et al., "Protein engineering of antibody binding sites: recovery of specific activity in an anti-digoxin single-chain Fv analogue produced in Escherichia coli," Proc. Natl. Acad. Sci. 85:5879-5883, 1988	
		HWANG et al., "Expression of Epidermal Growth Factor Receptors and C-ERBB-2 Proteins in Human Astrocytic Tumors," Kaohsiung Journal of Medical Sciences, 13(7):417-424, 1997	
		HYNES et al., "The biology of erbB-2/neu/HER-2 and its role in cancer," Biochimica et Biophysica Acta 1198:165-184, 1994	
		JACKSON et al., "Blockade of Epidermal Growth Factor- or Heregulin-Dependent ErbB2 Activation with the Anti-ErbB2 Monoclonal Antibody 2C4 Has Divergent Downstream Signaling and Growth Effects," Cancer Research 64(7):2601-2609, April 1, 2004	
		JACKSON-BOOTH et al., "Inhibition of the Biologic Response to Insulin-like Growth Factor I in MCF-7 Breast Cancer Cells by a New Monoclonal Antibody to the Insulin-like Growth Factor-I Receptor. The Importance of Receptor Down-regulation," Horm. Metab. Res. 35(11-23):850-856, November-December 2003	
		JAIN, "Barriers to Drug Delivery in Solid Tumors," Scientific American 271(1):58-65, 1994	
		JEROME et al., "Anti-Insulin-Like Growth Factor Strategies in Breast Cancer," Semin. Oncol. 31(1 Suppl 3):54-63, February 2004	
		JHABVALA-ROMERO et al., "Herstatin inhibits heregulin-mediated breast cancer cell growth and overcomes tamoxifen resistance in breast cancer cells that overexpress HER-2," Oncogene 22:8178-8186, 2003	

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		JIA et al., "Specific Tumoricidal Activity of a Secreted proapoptotic Protein Consisting of HER2 Antibody and Constitutively Active Caspase-3," Cancer Research 63(12):3257-3262, June 15, 2003	
		JOLLY, "Viral vector systems for gene therapy," Cancer Gene Therapy 1(1):51-64, March 1994	
		JUSTMAN et al., "Herstatin, an Autoinhibitor of the Human epidermal Growth Factor Receptor 2 Tyrosine Kinase, Modulates Epidermal Growth Factor Signaling Pathways Resulting in Growth Arrest," J. Biol. Chem. 277(23):20618-20624, 2002	
		KAPLITT et al., "Long-term gene expression and phenotypic correction using adeno-associated virus vectors in the mammalian brain," Nature Genetics 8(2):148-154, October 1994	
		KERN et al., "Inhibition of Human Lung Cancer Cell Line Growth by an Anti-p185(HER2) Antibody," American Journal of Respiratory Cell and Molecular Biology 9:448-454, 1993	
		KIMURA et al., "Retroviral Delivery of DNA into the Livers of Transgenic Mice Bearing Premalignant and Malignant Hepatocellular Carcinomas," Human Gene Therapy 5(7):845-852, July 1994	
		KIRSCH et al., "BMP-2 antagonists emerge from alterations in the low-affinity binding epitope for receptor BMPR-II," The EMBO Journal 19(13):3314-3324, 2000	
		KÖHLER et al., "Continuous cultures of fused cells secreting antibody of predefined specificity," Nature 256:495-497, 1975	
		KOZBOR et al., "The production of monoclonal antibodies from human lymphocytes," Immunology Today 4(3):72-79, 1983	
		KRAINER et al., "Tissue Expression and Serum Levels of HER-2/neu in Patients with Breast Cancer," Oncology 54:475-481, 1997	
		KRAUS et al., "Overexpression of the EGF receptor-related proto-oncogene erbB-2 in human mammary tumor cell lines by different molecular mechanisms," EMBO J. 6:605-610, 1987	
		KUMAGAI et al., "The role of distinct p185(neu) extracellular subdomains for dimerization with the epidermal growth factor (EGF) receptor and EGF-mediated signaling," Proc. Natl. Acad. Sci. 98(10):5526-5531, 2001	
		KUROKAWA, "Inhibition of HER2/neu (erbB-2) and mitogen-activated protein kinases enhances tamoxifen action against HER2-overexpressing, tamoxifen-resistant breast cancer cells," Cancer Res. 60:5887-5894, 2000	
		LANGTON et al., "An antigen immunologically related to the external domain of gp185 is shed from nude mouse tumors overexpressing the c-ERBB-2 (Her-2/Neu) oncogene," Canc. Res. 51:2593-2598, 1991	
		LAX et al., "Localization of a Major Receptor-Binding Domain for Epidermal Growth Factor by Affinity Labeling," Molecular and Cellular Biology 8(4):1831-1834, 1988	
		LEE et al., "Isolation and characterization of four alternate c-erbB3 transcripts expressed in ovarian carcinoma-derived cell lines and normal human tissues," Oncogene 16:3243-3252, 1998	
		LEE et al., "A Naturally Occurring Secreted Human ErbB3 Receptor Isoform Inhibits Heregulin-stimulated Activation of ErbB2, ErbB3, and ErbB4," Cancer Research 61:4467-4473, 2001	

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		LEE et al., "Requirement for neuregulin receptor erbB2 in neural and cardiac development," Nature 378:394-398, 1995	
		LEE et al., "Serum Tyrosine Kinase Activity and Neoplastic Disease," Recent Results in Cancer Research 113:32-40, 1989	
		LEITZEL et al., "Elevated Soluble c-erbB-2 Antigen Levels in the Serum and Effusions of a Proportion of Breast Cancer Patients," Journal of Clinical Oncology 10(9):1436-1443, 1992	
		LEMMON et al., "Two EGF molecules contribute additively to stabilization of the EGFR dimer," The EMBO Journal 16(2):281-294, 1997	
		LEWIS et al., "Differential responses of human tumor cell lines to anti-p185(HER2) monoclonal antibodies," Cancer Immunology Immunotherapy 37:255-263, 1993	
		LI et al., "Cytotoxicity of human prostate cancer cell lines in vitro and induction of apoptosis using <sup>213</sup> Bi-Herceptin alpha-conjugate," Cancer Letters 205(2):161-171, March 18, 2004	
		LIBERMANN et al., "Amplification, enhanced expression and possible rearrangement of EGF receptor gene in primary human brain tumours of glial origin," Nature 313: 144-147, 1985	
		LIN et al., "Characterization of tyrosyl kinase activity in human serum," J. Biol. Chem. 260(3) 1582-1587, 1985	
		LIN et al., "Developmental Expression of Tyrosyl Kinase Activity in Human Serum," Human Biology 59(3):549-556, 1987	
		LIN et al., "Disulfide-Linked and Noncovalent Dimers of p185(HER-2) in Human Breast Carcinoma Cells," Journal of Cellular Biochemistry 49(3):290-295, 1992	
		LIN et al., "The Epidermal Growth Factor Receptor from Prostate Cells Is Dephosphorylated by a Prostate-Specific Phosphotyrosyl Phosphatase," Mol. Cell Biol. 8(12): 5477-5485, December 1988	
		LIN et al., "Human prostatic acid phosphatase has phosphotyrosyl protein phosphatase activity," Biochem. J. 235:351-357, 1986	
		LIN et al., "Insulin and epidermal growth factor stimulate phosphorylation of p185(HER-2) in the breast carcinoma cell line, BT474," Molecular and Cellular Endocrinology 69(2-3):111-119, 1990	
		LIN et al., "A soluble protein related to the HER-2 proto-oncogene product is released from human breast carcinoma cells," Oncogene 6(4):639-643, 1991	
		LIN et al., "Tyrosyl Kinase Activity is Inversely Related to Prostatic Acid Phosphatase Activity in Two Human Prostate Carcinoma Cell Lines," Mol. Cell Biol. 6(12):4753-4757, December 1986	
		LIU et al., "MCF-7 breast cancer cells overexpressing transfected c-erbB-2 have an in vitro growth advantage in estrogen-depleted conditions and reduced estrogen-dependence and tamoxifen-sensitivity in vivo," Breast Cancer Res. Treatment 34:97-117, 1995	

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				First Named Inventor	Gail M. Clinton
				Art Unit	1643
				Examiner Name	Anne L. Holleran
Sheet	12	of	17	Attorney Docket Number	49321-16

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		LU et al., "Effect of Epidermal Growth Factor Receptor Inhibitor on Development of Estrogen Receptor-Negative Mammary Tumors," Journal of the National Cancer Institute 95(24):1825-1833, December 17, 2003	
		LU et al., "Insulin-Like Growth Factor-I Receptor Signaling and Resistance to Trastuzumab (Herceptin)," Journal of the National Cancer Institute 93(24):1852-1857, December 19, 2001	
		LU et al., "Molecular Mechanisms Underlying IGF-I-Induced Attenuation Of The Growth-Inhibitory Activity of Trastuzumab (Herceptin) On SKBR3 Breast Cancer Cells," Int. J. Cancer 108(3):334-341, January 20, 2004	
		LU et al., "Simultaneous Blockade of Both the Epidermal Growth Factor Receptor and the Insulin-like Growth Factor Receptor Signaling Pathways in Cancer Cells with a Fully Human Recombinant Bispecific Antibody," The Journal of Biological Chemistry 279(4):2856-2865, January 23, 2004	
		MAISONPIERRE et al., "Angiopoietin-2, a Natural Antagonist for Tie2 That Disrupts in vivo Angiogenesis," Science 277(5322):55-60, 1997	
		MALONEY, "An Anti-Insulin-like Growth Factor I Receptor Antibody That Is a Potent Inhibitor of Cancer Cell Proliferation," Cancer Research 63(16):5073-5083, August 15, 2003	
		MEDEN et al., "Elevated serum levels of a c-erbB-2 oncogene product in ovarian cancer patients and in pregnancy," J. Canc. Res. Clin. Oncol. 120:378-381, 1994	
		MEDEN et al., "Prognostic Significance of p105 (c-erbB-2, HER2/neu) Serum Levels in Patients with Ovarian Cancer," Anticancer Research 17:757-760, 1997	
		MILLER et al., "Regulation of HER2/neu gene expression (Review)," Oncology Reports 2:497-503, 1995	
		MIN et al., "Genetic Blockade of the Insulin-like Growth Factor-I Receptor: A Promising Strategy for Human Pancreatic Cancer," Cancer Research 63(19):6432-6441, October 1, 2003	
		MITSIADES et al., "Inhibition of the insulin-like growth factor receptor-1 tyrosine kinase activity as a therapeutic strategy for multiple myeloma, other hematologic malignancies, and solid tumors," Cancer Cell 5(3):221-230, March 2004	
		MOLINA et al., "NH <sub>2</sub> -terminal Truncated HER-2 Protein but not Full-Length Receptor is Associated with Nodal Metastasis in Human Breast Cancer," Clinical Cancer Research 8:347-353, 2002	
		MORRISON et al., "Chimeric Human Antibody Molecules: Mouse Antigen-Binding Domains with Human Constant Region Domains," Proc. Natl. Acad. Sci. 81:6851-6855, 1984	
		MOSCATELLO et al., "Transformation and altered signal transduction by a naturally occurring mutant EGF receptor," Oncogene 13:85-96, 1996	
		MYERS et al., "Elevated Serum Levels of p105(erbB-2) in Patients with Advanced-Stage Prostatic Adenocarcinoma," Int. J. Cancer (Pred. Oncol.) 69:398-402, 1996	
		NAHTA et al., "The HER-2-Targeting Antibodies Trastuzumab and Pertuzumab Synergistically Inhibit the Survival of Breast Cancer Cells," Cancer Research 64(7):2343-2346, April 1, 2004	
		NAIDU et al., "Antiproliferative and apoptotic effect of ascorbyl stearate in human glioblastoma multiforme cells: modulation of insulin-like growth factor-I receptor (IGF-IR) expression," Journal of Neuro-Oncology 54(1):15-22, August 2001	

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		NATALI et al., "Expression of the p185 Encoded by HER2 Oncogene in Normal and Transformed Human Tissues," Int. J. Cancer 45:457-461, 1990	
		NEUBERGER et al., "Recombinant antibodies possessing novel effector functions," Nature 312:604-608, 1984	
		NEUWELT et al., "Inhibition of brain tumor growth by Herstatin, an autoinhibitor of the EGF receptor family," Proceedings of the American Association for Cancer Research Annual Meeting, 44:1232, 2003 (abstract only)	
		NISHIKAWA et al., "A mutant epidermal growth factor receptor common in human glioma confers enhanced tumorigenicity," Proc. Natl. Acad. Sci. 91:7727-7731, August 1994	
		NISONOFF, "Idiotypes: Concepts and Applications," Journal of Immunology 147(8):2429-2438, 1991	
		OBRENOVICH et al., "Overexpression of GRK2 in Alzheimer Disease and in a Chronic Hypoperfusion Rat Model is an Early Marker of Brain Mitochondrial Lesions," Neurotoxicity Research 10(1):43-56, 2006	
		OLAYIOYE et al., "The ErbB signaling network: receptor heterodimerization in development and cancer," EMBO Journal 19(13):3159-3167, July 3, 2000	
		O'ROURKE et al., "Trans receptor inhibition of human glioblastoma cells by erbB family ectodomains," Proc. Natl. Acad. Sci. 94(7):3250-3255, 1997	
		PAVELIC et al., "Evidence for a Role of EGF Receptor in the Progression of Human Lung Carcinoma," Anticancer Research 13:1133-1138, 1993	
		PEGGRAM et al., "Biological Rationale for HER2/neu (c-erbB2) as a Target for Monoclonal Antibody Therapy," Seminars in Oncology 27(5)(Suppl. 9):13-19, 2000	
		PETCH et al., "A truncated, secreted form of the epidermal growth factor receptor is encoded by an alternatively spliced transcript in normal rat tissue," Mol. Cell. Biol. 10:2973-2982, 1990	
		PHILIP et al., "Efficient and Sustained Gene Expression in Primary T Lymphocytes and Primary and cultured Tumor Cells Mediated by Adeno-Associated Virus Plasmid DNA Complexed to Cationic Liposomes," Molecular and Cellular Biology 14(4):2411-2418, April 1994	
		PIETRAS et al., "HER-2 tyrosine kinase pathway targets estrogen receptor and promotes hormone-independent growth in human breast cancer cells," Oncogene 10:2435-2446, 1995	
		PINCKARD et al., "Factors Influencing The Immune Response. I. Effects Of The Physical State Of The Antigen And Of Lymphoreticular Cell Proliferation On The Response To Intravenous Injection Of Bovine Serum Albumin In Rabbits," Clin. Exp. Immunol. 2(3):331-341, May 1967	
		PUPA et al., "The extracellular domain of the c-erbB-2 oncoprotein is released from tumor cells by proteolytic cleavage," Oncogene 8:2917-2923, 1993	
		QIAN et al., "Intermolecular Association and Trans-phosphorylation of Different neu-Kinase Forms Permit SH2-dependent Signaling and Oncogenic Transformation," Oncogene 10:211-219, 1995	
		REINMUTH et al., "Blockade of Insulin-like Growth Factor I Receptor Function Inhibits Growth and Angiogenesis of Colon Cancer," Clinical Cancer Research 8(10):3259-3269, October 2002	

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		ROBBINS et al., "Antibodies to Covalent Aggregates of Insulin in Blood on Insulin-Using Diabetic Patients," Diabetes 36:838-841, July 1987	
		RUDIKOFF et al., "Single amino acid substitution altering antigen-binding specificity," Proc. Natl. Acad. Sci. 79:1979-1983, 1982	
		SACHDEV et al., "A Chimeric Humanized Single-Chain Antibody against the Type I Insulin-like Growth Factor (IGF) Receptor Renders Breast Cancer Cells Refractory to the Mitogenic Effects of IGF-I," Cancer Research 63(6):627-635, February 1, 2003	
		SALATINO et al., "Inhibition of in vivo breast cancer growth by antisense oligodeoxynucleotides to type I insulin-like growth factor receptor mRNA involves inactivation of ErbBs, PI-3K/Akt and p42/p44 MAPK signaling pathways but not modulation of progesterone receptor activity," Oncogene 23(30):5161-5174, July 1, 2004	
		SALISBURY et al., "Development of Molecular Agents for IGF Receptor Targeting," Horm. Metab. Res. 35(11-12):843-849, November-December 2003	
		SAMANI et al., "Inhibition of Carcinoma Cell Growth and Metastasis by a Vesicular Stomatitis Virus G-Pseudotyped Retrovector Expressing Type I Insulin-Like Growth Factor Receptor Antisense," Human Gene Therapy 12(16):1969-1977, November 1, 2001	
		SAMINI et al., "Loss of Tumorigenicity and Metastatic Potential in Carcinoma Cells Expressing the Extracellular Domain of the Type 1 Insulin-Like Growth Factor Receptor," Cancer Research 64(10):3380-3385, May 15, 2004	
		SCHALLER et al., "Therapy of metastatic breast cancer with humanized antibodies against the HER2 receptor protein," J. Cancer Res. Clin. Oncol. 125:520-524, 1999	
		SCHWEITZER et al., "Inhibition of Drosophila EGF receptor activation by the secreted protein Argos," Nature 376:699-702, 1995	
		SCOTLANDI et al., "Effectiveness of insulin-like growth factor I receptor antisense strategy against Ewing's sarcoma cells," Cancer Gene Therapy 9(3):296-307, March 2002	
		SCOTLANDI et al., "Expression Of An IGF-I Receptor Dominant Negative Mutant Induces Apoptosis, Inhibits Tumorigenesis And Enhances Chemosensitivity In Ewing's Sarcoma Cells," Int. J. Cancer 101(1):11-16, September 1, 2002	
		SEARCH REPORT: Supplementary Partial European Search Report, Application Number EP 00930067, 7/8/02, 3 pages	
		SEGATTO et al., "Different Structural Alterations Upregulate In Vitro Tyrosine Kinase Activity and Transforming Potency of the erbB-2 Gene," Mol. Cell. Biol. 8(12):5570-5574, 1988	
		SEQUENCE SEARCH RESULTS, Issued Patents database, "us-10-204-102a-1.ra1", p. 1-2	
		SEVERINO et al., "Rapid loss of oestrogen and progesterone receptors in human leiomyoma and myometrial explant cultures," Mol. Human Repro. 2(11):823-828, 1996	
		SHAMIEH et al., "The intron 8-encoded domain of Herstatin encodes a receptor binding module that is required for erbB receptor inhibition," Proceedings on the American Association for Cancer Research 44:1233, 2003 (abstract only)	

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		SHARP et al., "Classification of introns: U2-type or U12-type," Cell 91:875-879, 1997	
		SHEPARD et al., "Monoclonal Antibody Therapy of Human Cancer: Taking the HER2 Protooncogene to the Clinic," J. Clin. Immunol. 11(3):117-127, 1991	
		SLAMON et al., "The Future of ErbB-1 and ErbB-2 Pathway Inhibition in Breast Cancer: Targeting Multiple Receptors," Oncologist 9(Suppl 3):1-3, 2004	
		SLAMON et al., "Human Breast Cancer: Correlation of Relapse and Survival with Amplification of the HER-2/neu Oncogene," Science 235(4785):177-182, 1987	
		SLAMON et al., "Studies of the HER-2/neu Proto-Oncogene in Human Breast and Ovarian Cancer," Science 244(4905):707-712, 1989	
		SMITH, "Comparison of Biosequences," Advances in Applied Mathematics 2:482-489, 1981	
		SMITH et al., "Human Interleukin 4: The Solution Structure of a Four-helix Bundle Protein," J. Mol. Biol. 244:899-904, 1992	
		STANCOVSKI et al., "Mechanistic aspects of the opposing effects of monoclonal antibodies to the ERBB2 receptor on tumor growth," Proc. Natl. Acad. Sci. 88:8691-8695, 1991	
		STAVEROSKY et al., "Herstatin, an autoinhibitor of the epidermal growth factor (EGF) receptor family, blocks the intracranial growth of glioblastoma," Clin. Cancer Res. 11(1):335-340, 2005	
		STEBBING et al., "Herceptin (trastuzumab) in advanced breast cancer," Cancer Treatment Reviews 26(4):287-290, August 2000	
		Stedman's Medical Dictionary 27 <sup>th</sup> Edition, Lippicott Williams & Wilkins, 2000, definition for astrocyte	
		Stedman's Medical Dictionary 27 <sup>th</sup> Edition, Lippicott Williams & Wilkins, 2000, definition for glial	
		STEIN et al., "Evolutionary Analysis of the ErbB Receptor and Ligand Families," J. Mol. Evol. 50(5):397-412, May 2000	
		STERN et al., "p185, a product of the neu proto-oncogene, is a receptor like protein associated with tyrosine kinase activity," Mol. Cell. Biol. 6:1729-1740, 1986	
		ST.-JACQUES et al., "Molecular characterization and in situ localization of murine endoglin reveal that it is a transforming growth factor-beta binding protein of endothelial and stromal cells," Endocrinology 134:2645-2657, 1994	
		STROBEL et al., "Beta-1 Integrins Partly Mediate Binding of Ovarian Cancer Cells to Peritoneal Mesothelium in Vitro," Gynecologic Oncology 73:362-367, 1999	
		SURMACZ, "Growth factor receptors as therapeutic targets: strategies to inhibit the insulin-like growth factor I receptor," Oncogene 22(42):6589-6597, September 29, 2003	
		TAKEDA et al., "Construction of chimaeric processed immunoglobulin genes containing mouse variable and human constant region sequences," Nature 314:452-454, 1985	
		TAL et al., "Human HER2 (neu) promoter: evidence for multiple mechanisms for transcriptional initiation, Mol. Cell. Biol. 7(7):2597-2601, 1987	

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		TANNER et al., "Dimerization of the Extracellular Domain of the Receptor for Epidermal Growth Factor Containing the Membrane-spanning Segment in Response to Treatment with Epidermal Growth Factor," Journal of Biological Chemistry 274(50):35985-35990, 1999	
		TOPP et al., "Antibody transport in cultured tumor cell layers," Journal of Controlled Release 53:15-23, 1998	
		TYSON et al., "Expression and amplification of the HER-2/neu (c-erbB-2) protooncogene in epithelial ovarian tumors and cell lines," Am. J. Obstet. Gynecol. 165(3):640-646, 1991	
		TZAHAR et al., "Bivalence of EGF-like ligands drives the ErbB signaling network," EMBO Journal 16(16):4938-4950, 1997	
		TZAHAR et al., "The ErbB-2/HER2 oncogenic receptor of adenocarcinomas: from orphanhood to multiple stromal ligands," Biochimica et Biophysica Acta 1377(1):M25-M37, February 20, 1998	
		ULLRICH et al., "Human epidermal growth factor receptor cDNA sequence and aberrant expression of the amplified gene in A431 epidermoid carcinoma cells," Nature 309:418-425, 1984	
		VALERON et al., "Validation of a differential PCR and an ELISA procedure in studying HER-2/neu status in breast cancer," Int. J. Cancer 65:129-133, 1996	
		VAN OSTADE et al., "Human TNF mutants with selective activity on the p55 receptor," Nature 361(6409):266-269, January 21, 1993	
		VECCHI et al., "Constitutive proteolysis of the ErbB-4 receptor tyrosine kinase by a unique, sequential mechanism," J. Cell. Biol. 139:995-1003, 1997	
		VECCHI et al., "Selective cleavage of the heregulin receptor ErbB-4 by protein kinase C activation," J. Biol. Chem. 271:18989-18995, 1996	
		WANG et al., "Insulin-Like Growth Factor Receptor-1 as an Anti-Cancer Target: Blocking Transformation and Inducing Apoptosis," Current Cancer Drug Targets 2:191-207, 2002	
		WARD et al., "Binding activities of a repertoire of single immunoglobulin variable domains secreted from Escherichia coli," Nature 341:544-546, 1989	
		WINER et al., "New Combinations with Herceptin® in Metastatic Breast Cancer," Oncology 61(Supplement 2):50-57, 2001	
		WOFFENDIN et al., "Nonviral and viral delivery of a human immunodeficiency virus protective gene into primary human T cells," Proc. Natl. Acad. Sci. 91(24):11581-11585, November 22, 1994	
		WOLTJER et al., "Direct identification of residues of the epidermal growth factor receptor in close proximity to the amino terminus of bound epidermal growth factor," Proc. Natl. Acad. Sci. 89(16):7801-7805, 1992	
		WU et al., "Human epidermal growth factor receptor residue covalently cross-linked to epidermal growth factor," Proc. Natl. Acad. Sci. 87:3151-3155, 1990	
		WU et al., "Incorporation of Adenovirus into a Ligand-based DNA Carrier System Results in Retention of Original Receptor Specificity and Enhances Targeted Gene Expression," The Journal of Biological Chemistry 269(15):11542-11546, April 15, 1994	

Examiner Signature	Date
	Considered

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

**Complete if Known**

Application Number	09/506,079
Filing Date	February 16, 2000
First Named Inventor	Gail M. Clinton
Art Unit	1643
Examiner Name	Anne L. Holleran
Attorney Docket Number	49321-16

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Examiner Signature		Date Considered	
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